# Alzheimer disease

Alzheimer disease is a degenerative disease of the brain that causes dementia, which is a gradual loss of memory, judgment, and ability to function. This disorder usually appears in people older than age 65, but less common forms of the disease appear earlier in adulthood.

Memory loss is the most common sign of Alzheimer disease. Forgetfulness may be subtle at first, but the loss of memory worsens over time until it interferes with most aspects of daily living. Even in familiar settings, a person with Alzheimer disease may get lost or become confused. Routine tasks such as preparing meals, doing laundry, and performing other household chores can be challenging. Additionally, it may become difficult to recognize people and name objects. Affected people increasingly require help with dressing, eating, and personal care.

As the disorder progresses, some people with Alzheimer disease experience personality and behavioral changes and have trouble interacting in a socially appropriate manner. Other common symptoms include agitation, restlessness, withdrawal, and loss of language skills. People with this disease usually require total care during the advanced stages of the disease. Affected individuals usually survive 8 to 10 years after the appearance of symptoms, but the course of the disease can range from 1 to 25 years. Death usually results from pneumonia, malnutrition, or general body wasting (inanition).

Alzheimer disease can be classified as early-onset or late-onset. The signs and symptoms of the early-onset form appear before age 65, while the late-onset form appears after age 65. The early-onset form is much less common than the late-onset form, accounting for less than 5 percent of all cases of Alzheimer disease.

# Frequency

Alzheimer disease currently affects an estimated 2.4 million to 4.5 million Americans. Because the risk of developing Alzheimer disease increases with age and more people are living longer, the number of people with this disease is expected to increase significantly in coming decades.

# Genetic Changes

Most cases of early-onset Alzheimer disease are caused by gene mutations that can be passed from parent to child. Researchers have found that this form of the disorder can result from mutations in one of three genes: *APP*, *PSEN1*, or *PSEN2*. When any of these genes is altered, large amounts of a toxic protein fragment called amyloid beta peptide are produced in the brain. This peptide can build up in the brain to form clumps

called amyloid plaques, which are characteristic of Alzheimer disease. A buildup of toxic amyloid beta peptide and amyloid plaques may lead to the death of nerve cells and the progressive signs and symptoms of this disorder.

Some evidence indicates that people with Down syndrome have an increased risk of developing Alzheimer disease. Down syndrome, a condition characterized by intellectual disability and other health problems, occurs when a person is born with an extra copy of chromosome 21 in each cell. As a result, people with Down syndrome have three copies of many genes in each cell, including the *APP* gene, instead of the usual two copies. Although the connection between Down syndrome and Alzheimer disease is unclear, the production of excess amyloid beta peptide in cells may account for the increased risk. People with Down syndrome account for less than 1 percent of all cases of Alzheimer disease.

The causes of late-onset Alzheimer disease are less clear. The late-onset form does not clearly run in families, although clusters of cases have been reported in some families. This disorder is probably related to variations in one or more genes in combination with lifestyle and environmental factors. A gene called *APOE* has been studied extensively as a risk factor for the disease. In particular, a variant of this gene called the e4 allele seems to increase an individual's risk for developing late-onset Alzheimer disease. Researchers are investigating many additional genes that may play a role in Alzheimer disease risk.

#### Inheritance Pattern

The early-onset form of Alzheimer disease is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the altered gene from one affected parent.

The inheritance pattern of late-onset Alzheimer disease is uncertain. People who inherit one copy of the *APOE* e4 allele have an increased chance of developing the disease; those who inherit two copies of the allele are at even greater risk. It is important to note that people with the *APOE* e4 allele inherit an increased risk of developing Alzheimer disease, not the disease itself. Not all people with Alzheimer disease have the e4 allele, and not all people who have the e4 allele will develop the disease.

### Other Names for This Condition

- AD
- Alzheimer dementia (AD)
- Alzheimer sclerosis
- Alzheimer syndrome
- Alzheimer-type dementia (ATD)

- Alzheimer's Disease
- DAT
- familial Alzheimer disease (FAD)
- Presenile and senile dementia
- Primary Senile Degenerative Dementia
- SDAT

## **Diagnosis & Management**

These resources address the diagnosis or management of Alzheimer disease:

- Alzheimer's Disease Research Center, Washington University School of Medicine http://alzheimer.wustl.edu/
- American Psychiatric Association: Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias http://psychiatryonline.org/pb/assets/raw/sitewide/practice\_guidelines/guidelines/ alzheimerwatch.pdf
- GeneReview: Alzheimer Disease Overview https://www.ncbi.nlm.nih.gov/books/NBK1161
- GeneReview: Early-Onset Familial Alzheimer Disease https://www.ncbi.nlm.nih.gov/books/NBK1236
- Genetic Testing Registry: Alzheimer disease 2 https://www.ncbi.nlm.nih.gov/qtr/conditions/C1863051/
- Genetic Testing Registry: Alzheimer disease, type 3 https://www.ncbi.nlm.nih.gov/gtr/conditions/C1843013/
- Genetic Testing Registry: Alzheimer disease, type 4 https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847200/
- Genetic Testing Registry: Alzheimer's disease https://www.ncbi.nlm.nih.gov/gtr/conditions/C0002395/
- MedlinePlus Encyclopedia: Alzheimer's Disease https://medlineplus.gov/ency/article/000760.htm
- Michigan Alzheimer's Disease Research Center http://alzheimers.med.umich.edu/
- University of California Davis Alzheimer's Disease Center http://www.ucdmc.ucdavis.edu/alzheimers/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests https://medlineplus.gov/diagnostictests.html
- Drug Therapy https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling https://medlineplus.gov/geneticcounseling.html
- Palliative Care https://medlineplus.gov/palliativecare.html

## **Additional Information & Resources**

## **MedlinePlus**

- Encyclopedia: Alzheimer's Disease https://medlineplus.gov/ency/article/000760.htm
- Health Topic: Alzheimer's Caregivers https://medlineplus.gov/alzheimerscaregivers.html
- Health Topic: Alzheimer's Disease https://medlineplus.gov/alzheimersdisease.html

## Genetic and Rare Diseases Information Center

- Alzheimer disease https://rarediseases.info.nih.gov/diseases/10254/alzheimer-disease
- Familial Alzheimer disease https://rarediseases.info.nih.gov/diseases/632/familial-alzheimer-disease

#### Additional NIH Resources

- National Institute of Neurological Disorders and Stroke https://www.ninds.nih.gov/Disorders/All-Disorders/Alzheimers-Disease-Information-Page
- National Institute on Aging: Alzheimer's Disease Education and Referral Center https://www.nia.nih.gov/alzheimers
- National Institute on Aging: Alzheimer's Disease Genetics Fact Sheet https://www.nia.nih.gov/alzheimers/publication/alzheimers-disease-genetics-fact-sheet

- NIH Press Release: Scientists Isolate a Toxic Key to Alzheimer's Disease in Human Brains (June 22, 2008)
   https://www.nih.gov/news-events/news-releases/scientists-isolate-toxic-keyalzheimers-disease-human-brains
- NIH SeniorHealth https://nihseniorhealth.gov/alzheimersdisease/whatisalzheimersdisease/01.html

#### **Educational Resources**

- Cleveland Clinic Health Information Center: Alzheimer's Disease http://my.clevelandclinic.org/health/articles/alzheimers-and-dementia-overview
- Cleveland Clinic Health Information Center: Alzheimer's Disease and Down Syndrome http://my.clevelandclinic.org/health/articles/alzheimers-disease-and-downsyndrome
- Disease InfoSearch: Alzheimer Disease http://www.diseaseinfosearch.org/Alzheimer+Disease/349
- Disease InfoSearch: Alzheimer Disease Familial http://www.diseaseinfosearch.org/Alzheimer+Disease+Familial/350
- Emory University School of Medicine http://genetics.emory.edu/documents/resources/Emory\_Human n Genetics Family History Alzheimer Disease.PDF
- Genetic Science Learning Center, University of Utah http://learn.genetics.utah.edu/content/disorders/multifactorial/
- Joseph and Kathleen Bryan Alzheimer's Disease Research Center, Duke University Medical Center https://adrc.mc.duke.edu/
- MalaCards: alzheimer disease http://www.malacards.org/card/alzheimer\_disease
- MalaCards: alzheimer disease risk factor http://www.malacards.org/card/alzheimer\_disease\_risk\_factor\_apoe\_genotype
- Merck Manual Consumer Version: Alzheimer Disease Quick Facts http://www.merckmanuals.com/home/resources/quick-facts/alzheimer-disease-quick-facts
- Merck Manual Consumer Version: Overview of Delirium and Dementia http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/ delirium-and-dementia/overview-of-delirium-and-dementia

- Orphanet: Early-onset autosomal dominant Alzheimer disease http://www.orpha.net/consor/cgi-bin/OC\_Exp.php?Lng=EN&Expert=1020
- Your Genes Your Health from Cold Spring Harbor Laboratory http://www.ygyh.org/alz/whatisit.htm

# Patient Support and Advocacy Resources

- Alzheimer Research Forum http://www.alzforum.org/
- Alzheimer's Association http://www.alz.org/
- Alzheimer's Foundation of America http://www.alzfdn.org/
- Family Caregiver Alliance https://www.caregiver.org/alzheimers-disease-caregiving
- National Organization for Rare Disorders (NORD)
   https://rarediseases.org/rare-diseases/alzheimers-disease/

## GeneReviews

- Alzheimer Disease Overview https://www.ncbi.nlm.nih.gov/books/NBK1161
- Early-Onset Familial Alzheimer Disease https://www.ncbi.nlm.nih.gov/books/NBK1236

# **Genetic Testing Registry**

- Alzheimer disease 2 https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863051/
- Alzheimer disease, type 3 https://www.ncbi.nlm.nih.gov/gtr/conditions/C1843013/
- Alzheimer disease, type 4 https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847200/
- Alzheimer's disease https://www.ncbi.nlm.nih.gov/gtr/conditions/C0002395/

# ClinicalTrials.gov

ClinicalTrials.gov
 https://clinicaltrials.gov/ct2/results?cond=%22Alzheimer+disease%22

## Scientific Articles on PubMed

PubMed

https://www.ncbi.nlm.nih.gov/pubmed?term=%28Alzheimer+Disease%5BMAJR%5D%29+AND+%28%28Alzheimer+disease%5BTI%5D%29+OR+%28Alzheimer's +disease%5BTI%5D%29%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+180+days%22%5Bdp%5D

### OMIM

- ALZHEIMER DISEASE http://omim.org/entry/104300
- ALZHEIMER DISEASE 2 http://omim.org/entry/104310
- ALZHEIMER DISEASE 3 http://omim.org/entry/607822
- ALZHEIMER DISEASE 4 http://omim.org/entry/606889

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